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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/809,269	03/24/2004	Ian G. Brown	IB-1888	6914
8076	7590	03/05/2009	EXAMINER	
LAWRENCE BERKELEY NATIONAL LABORATORY ONE CYCLOTRON ROAD, MAIL STOP 90B UNIVERSITY OF CALIFORNIA BERKELEY, CA 94720			BEISNER, WILLIAM H	
			ART UNIT	PAPER NUMBER
			1797	
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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/809,269	BROWN ET AL.	
	Examiner	Art Unit	
	WILLIAM H. BEISNER	1797	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1) Responsive to communication(s) filed on 15 December 2008.
 2a) This action is FINAL. 2b) This action is non-final.
 3) Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4) Claim(s) 1-5 and 7-36 is/are pending in the application.
 4a) Of the above claim(s) _____ is/are withdrawn from consideration.
 5) Claim(s) _____ is/are allowed.
 6) Claim(s) 1-5 and 7-36 is/are rejected.
 7) Claim(s) _____ is/are objected to.
 8) Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9) The specification is objected to by the Examiner.
 10) The drawing(s) filed on _____ is/are: a) accepted or b) objected to by the Examiner.
 Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
 Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
 11) The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12) Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
 a) All b) Some * c) None of:
 1. Certified copies of the priority documents have been received.
 2. Certified copies of the priority documents have been received in Application No. _____.
 3. Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) <input type="checkbox"/> Notice of References Cited (PTO-892)	4) <input type="checkbox"/> Interview Summary (PTO-413)
2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948)	Paper No(s)/Mail Date. _____ .
3) <input type="checkbox"/> Information Disclosure Statement(s) (PTO/SB/08)	5) <input type="checkbox"/> Notice of Informal Patent Application
Paper No(s)/Mail Date _____.	6) <input type="checkbox"/> Other: _____ .

DETAILED ACTION

Continued Examination Under 37 CFR 1.114

1. A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on 12/15/2008 has been entered.

Claim Objections

2. Claim 7 is objected to because of the following informalities: Claim 7 depends from canceled claim 6. The claim will be treated as though it depends from claim 5. Appropriate correction is required.

Claim Rejections - 35 USC § 103

3. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

4. The factual inquiries set forth in *Graham v. John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.

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2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

5. This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

6. Claims 1, 35 and 36 are rejected under 35 U.S.C. 103(a) as being unpatentable over Kovacs et al.(US 5,981,268) in view of either Lu et al.(Bio-Medical Materials and Engineering) or Franks (US 4,968,623).

The reference of Kovacs et al. discloses a chip platform device that includes a CCD detector array (Fig.5:57), a thin protective film (Fig.5:58) over the CCD, and an insulating material (Fig.5:55) for insulating CCD electronics from a cell culture.

Claim 1 differs by reciting that the chip platform also includes a thin patterned film applied to the protective film.

The references of Lu et al. (See the abstract) and Franks (See the abstract) disclose that it is known in the cell culture art to employ a thin film of diamond-like carbon material to improve cell adhesion to a culture surface.

In view of any of these teachings, it would have been obvious to one of ordinary skill in the art at the time the invention was made to provide the detector array of the primary reference with a thin film of diamond-like carbon material to improve cell adhesion to the surface of the detector array.

With respect to claim 35, the references of Lu et al. and Franks disclose the use of diamond-like carbon.

With respect to claim 36, the use of culture adhesion proteins is notoriously well known in the art to facilitate and/or selectively culture cells on a culture surface. As a result, it would have been obvious to one of ordinary skill in the art to provide the device of the modified primary reference with culture adhesion proteins for the known and expected result of manipulating and/or facilitating the adhesion of the cultured cells to the detector surface.

7. Claims 2-5 and 7-34 are rejected under 35 U.S.C. 103(a) as being unpatentable over Kovacs et al.(US 5,981,268) in view of either Lu et al.(Bio-Medical Materials and Engineering) or Franks (US 4,968,623) taken further in view of Miyamoto (US 5,702,915).

The combination of the reference of Kovacs et al. with either of Lu et al. or Franks has been discussed above.

Claims 14 and 22 differ by reciting that the chip platform is provided in combination with an electrical connection system and image and/or signal processing means connected to the connection system. Claim 14 further recites an illumination source.

While the reference of Kovacs et al. discloses the use of both microelectrodes and CCD in the detection array, the reference is silent with respect to the imaging electronics and/or processors, including an illumination source.

The reference of Miyamoto discloses that it is known in the cell culture art to interface a cell culture with a CCD array (1) wherein the detection system includes control and/or processing electronics (8-10). The device also includes an illumination source (6).

In view of this disclosure, it would have been obvious to one of ordinary skill in the art at the time the invention was made to provide the imaging electronics disclosed by the reference of Miyamoto in combination with the CCD sensors disclosed by the reference of Kovacs et al. for the known and expected result of providing an art recognized means for interfacing the CCD of the primary reference with an image processing and control system.

With respect to the pixel size recited in claims 2 and 33, if not inherently met, it would have been obvious to one of ordinary skill in the art to optimize the size of the pixels based merely on the size of the cells intended to be used in the detector system.

With respect to claim 3, if the claimed film structure is not inherently met, it would have been obvious to one of ordinary skill in the art to determine the optimum manner in which to provide the film layers.

With respect to claims 4, 24 and 25, the reference of Kovacs et al. discloses that film layer (58) can be silicon nitride (See column 12, lines 20-25).

With respect to claim 5, if the claimed film structure is not inherently met, it would have been obvious to one of ordinary skill in the art to determine the optimum thickness of the film while maintaining the required functions of the sensor system.

With respect to claim 34, the references of Lu et al. or Franks disclose that the film is made of diamond-like carbon.

With respect to claim 7, if the claimed film structure is not inherently met, it would have been obvious to one of ordinary skill in the art to determine the optimum thickness of the film while maintaining the required functions of the sensor system.

With respect to claims 8, 26 and 27, the reference of Kovacs et al. discloses a number of insulation materials that can be used (See column 13, lines 35-46).

With respect to claims 15 and 23, the detector chip is capable of being detachable from the other system components.

With respect to claims 13 and 16, the reference of Kovacs et al. discloses that the device also include microelectrode structures formed on the device (See Figure 5, elements 52 and 56). Whether the electrodes are formed by etching the film layer (58) or by forming the electrode layer on the surface of film (58) would have been well within the purview of one having ordinary skill in the art while maintaining the function of the detection device.

With respect to claims 9-11, 17 and 18, the use of culture adhesion proteins is notoriously well known in the art to facilitate and/or selectively culture cells on a culture surface. As a result, it would have been obvious to one of ordinary skill in the art to provide the device of the modified primary reference with culture adhesion proteins for the known and expected result of manipulating and/or facilitating the adhesion of the cultured cells to the detector surface.

With respect to claim 20, use of the device in the manner suggested by the prior art combination, would result in the method steps recited in claim 20.

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With respect to claims 19, 21, 28 and 29, the device is capable of being used with cardiac cells. Note, the cells are considered material work on and do not further distinguish the structure of the claimed device.

With respect to claim 12, the reference of Kovacs et al. (See column 15, lines 53-63) discloses environmental control of the culture conditions.

With respect to claim 30, the reference of Miyamoto discloses the use of illumination source (6).

With respect to claims 31 and 32, the reference of Kovacs et al. discloses control electronics for applying voltage to the microelectrode array (See column 11, lines 48-60).

8. With respect to the rejection of Claim 1 under 35 U.S.C. 103(a) as being unpatentable over Kovacs et al.(US 5,981,268) in view of Lu et al.(Bio-Medical Materials and Engineering) or Franks (US 4,968,623), Applicants argue that the rejection is improper for the following reasons (See pages 7-9 of the response filed 12/15/2008):

"Applicants disagree that the two cited references, Luo et al. or Franks et al., disclose patterning the thin-film of diamond-like carbon (DLC) material.

While both references teach the use of DLC as a biologically compatible material suitable for use in cell culture, neither Luo et al. or Franks et al., nor any other cited reference, teach that application of DLC could be used to direct or pattern cell growth in a manner as Applicants have claimed. This feature is discussed specifically on page 12 of Applicants' specification and shown below.

"The patterning of film 30 is designed to control the connections between neuronal cells in predetermined ways. The material used in patterned film 30 is designed to facilitate neuronal attachment and growth, so that the areas of the device lacking patterned film 30 have essentially no neuronal growth.

Accordingly, a neuronal body may be selected for engagement by a dendrite at a pre-determined distance from the center of the neuron by virtue of the arrangement of patterned film 30. The patterned film 30 may also be formed of an electrically conductive metal to be useful for delivering an electrical signal to a pre-selected neuron."

*Applicants also point to Figure 6, which shows patterned growth of neurons on DLC while there is little to no growth on areas with no DLC. To establish *prima facie* obviousness of a claimed invention, all the claim limitations must be taught or suggested by the prior art. *In re Royka*, 490 F.2d 981, 180 USPQ 580 (CCPA 1974). Applicants respectfully submit that Kovacs et al. does not teach or suggest a cell culture apparatus having a thin patterned film that patterns cell growth, as claimed by Applicants. As such, the Examiner has failed to establish a *prima facie* case of obviousness with regard to claim 1, because the combination of Kovacs et al. in view of Franks et al. or Luo et al. does not teach each and every feature of Applicants' claimed invention.*

Furthermore, there is no teaching, suggestion or motivation to combine these two references with Kovacs et al. to make Applicants' claimed invention. Franks et al. and Luo et al. show examples of using DLC in common cell culture containers such as, vials and microtiter plates as shown in Figure 1 and 2 respectively in Franks et al. In Kovacs et al. the cells are grown either directly on the microelectrode array or in Petri dishes placed on the microelectrodes. Since according to Kovacs et al. the cells were allowed to adhere to the microelectrodes (col. 15, line 53), there would have been no motivation to use another patterned layer or film to pattern cell growth since it was not known that diamond-like carbon patterned cell growth as described in the present specification.

Since according to Kovacs et al. the cells were allowed to adhere to the microelectrodes (col. 15, line 53), there would have been no motivation to use another patterned layer or film to pattern cell growth since it was not known that diamond-like carbon patterned cell growth as described in the present specification. Furthermore, it would have been appreciated by one having skill in the art, that such microelectrode arrays do not react to cell culture media and are not extremely sensitive to exposure to cell culture media as a CCD optical array. Thus, Applicants assert that it would not have been obvious to use a patterned film of diamond-like carbon to pattern cell growth directly on a CCD array with only thin films to protect the detector array as described in Applicants' claims.

Thus, Applicants assert that it was not obvious to use a patterned film of diamond-like carbon to pattern cell growth on a detector array. Therefore, Applicants respectfully request that the rejection be withdrawn. In light of the foregoing arguments, Applicants respectfully request that the rejection of claim 1 under 35 U.S.C. § 103 be withdrawn and the claim allowed."

In response to applicant's argument that the references fail to show certain features of applicant's invention, it is noted that the features upon which applicant relies (i.e., the cell patterning disclosed in the instant specification) are not recited in the rejected claim(s).

Although the claims are interpreted in light of the specification, limitations from the specification

are not read into the claims. See *In re Van Geuns*, 988 F.2d 1181, 26 USPQ2d 1057 (Fed. Cir. 1993). Note the instant claims are not commensurate in scope with the arguments with respect to the patterning required of the instant invention when compared with the teachings of the prior art references of Lu et al. and Franks.

In response to applicant's argument that there is no suggestion to combine the references, the examiner recognizes that obviousness can only be established by combining or modifying the teachings of the prior art to produce the claimed invention where there is some teaching, suggestion, or motivation to do so found either in the references themselves or in the knowledge generally available to one of ordinary skill in the art. See *In re Fine*, 837 F.2d 1071, 5 USPQ2d 1596 (Fed. Cir. 1988) and *In re Jones*, 958 F.2d 347, 21 USPQ2d 1941 (Fed. Cir. 1992). In this case, it would have been obvious to one of ordinary skill in the art at the time the invention was made to provide the detector array of the primary reference with a thin film of diamond-like carbon material to improve cell adhesion to the surface of the detector array.

In response to applicant's argument that one of ordinary skill in the art would have no motivation to combine the references for the reasons set forth in the instant application, the fact that applicant has recognized another advantage which would flow naturally from following the suggestion of the prior art cannot be the basis for patentability when the differences would otherwise be obvious. See *Ex parte Obiaya*, 227 USPQ 58, 60 (Bd. Pat. App. & Inter. 1985).

9. Claims 2-33 are rejected under 35 U.S.C. 103(a) as being unpatentable over Kovacs et al.(US 5,981,268) in view of any of Brown et al.(LDRD Annual Report); Lu et al.(Bio-Medical Materials and Engineering) or Franks (US 4,968,623) taken further in view of Miyamoto (US

5,702,915), Applicants argue that the rejection is improper for the following reasons (See pages 9-10 of the response filed 3/18/2008):

"The Brown et al. reference was explicitly removed from the previous rejection. Because it would be improper for the Examiner to cite the Brown et al. for rejection of claims 2-33 under 35 U.S.C. § 103(a), Applicants do not include it in the analysis below. Applicants request that the Examiner confirm that the Brown et al. reference has been withdrawn for the present rejection of claims 2-33.

Applicants disagree with the Examiner's reading of Miyamoto as disclosing "that it is known in the cell culture art to interface a cell culture with a CCD array (1)..." Office Action at 5. Indeed, Miyamoto states that "[a]fter charge coupled device (CCD) have been made available, the element for taking photographs of images of a solid has developed and has been enormously improved... Because of these advantage[s], the element for taking photographs of images of a solid is taking over camera tubes in the field of broadcasting and so on." Miyamoto clearly is referring to using a CCD to take photographs of a solid and cell activity (col. 1, line 54) and not referring to any known technique of "interfac[ing]" cells with a CCD array.

Neither does Miyamoto teach or suggest interfacing cells with a CCD array as claimed by Applicants. Miyamoto teaches the use of a cell culture container positioned on the upper surface of a solid-state area image pickup element, but does not teach or suggest the use of a thin protective film over the CCD and/or a thin patterned film to pattern cellular growth. Again, for the reasons given above, the cited references of Kovacs et al, Luo et al, and Franks et al. do not teach, suggest or motivate the combination of these elements to make Applicants' claimed invention. Applicants use a thin protective film of micron layer thickness as opposed to the cell culture containers taught by these four cited references which feature centimeter thickness. Heretofore, it was not contemplated that thin films could be used and that cells would remain viable for long-term growth (upwards of days and weeks at a time).

Applicants submit that the aspects of the invention of growing cells on a CCD array, using thin film of micron thickness and growing cells in a pattern for long-term growth were unexpected results and demonstrated technology that is a leap forward, not an obvious change from the prior art. Prior to Applicants claimed invention, this invention had not been shown to be possible. Applicants submit that the Examiner has not appreciated this unexpected result of patterning cell growth on a CCD array for long-term growth. Certainly the Examiner can at least appreciate the sensitivity of optical CCD arrays would normally require that the prevention of fluid contact with a CCD array. Growing cells on an optical CCD array for long-term growth is a feat Applicants have demonstrated and so claim. This is well-beyond taking pictures of cells through a cell plate as suggested by Miyamoto. Moreover making films that are both transparent, pattern

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cell growth and are not permeable to the cell media would not be obvious choices to allow direct interfacing and growth on a CCD array. The present invention represents a leap forward, not just an obvious step away from these references. As evidence of this, Applicants attached a copy of a special press release which describes that Applicants received special DARPA funding and R&D 100 awards for this technology to the previous response. Furthermore, the licensee of this technology has received continued DARPA funding for the development of this technology.

Thus, Applicants assert that it was not obvious to combine these references to use a thin protective film directly over the CCD or to use a thin patterned film such as diamond-like carbon to pattern cell growth on a detector array. Therefore, Applicants respectfully request that the rejection be withdrawn. In light of the foregoing arguments, Applicants respectfully request that the rejection of claims 2-33 under 35 U.S.C. § 103 be withdrawn and the claims allowed.”

In response to applicant's comments concerning the Brown et al. reference, the rejections of claims 2-33 using this reference have been withdrawn for the same reasons as set forth in the Final Office action dated 6/27/2008.

In response to applicant's arguments against the references individually, one cannot show nonobviousness by attacking references individually where the rejections are based on combinations of references. See *In re Keller*, 642 F.2d 413, 208 USPQ 871 (CCPA 1981); *In re Merck & Co.*, 800 F.2d 1091, 231 USPQ 375 (Fed. Cir. 1986). In this case, the combination of the references of Kovacs et al. with Lu et al. or Franks suggests interfacing a CCD detector device with a culture substrate. The reference of Miyamoto is relied upon as a teaching of using that additionally claimed imaging structures when using a CCD detection device as suggested by the combination of the references of Kovacs et al. and either Lu et al. or Frank. Again the combination of the references of Kovacs et al. and either Lu et al. or Frank is considered to be proper and meet the instant claim language for the reasons all ready set forth above with respect to the arguments against claim 1.

With respect to Applicant's comments concerning unexpected results, these comments are not found persuasive because the evidence has not been presented in the form of a declaration under 37 CFR 1.132 and/or the instant claims do not appear to commensurate in scope with applicant's comments as set forth previously above.

Conclusion

10. Any inquiry concerning this communication or earlier communications from the examiner should be directed to WILLIAM H. BEISNER whose telephone number is (571)272-1269. The examiner can normally be reached on Tues. to Fri. and alt. Mon. from 6:15am to 3:45pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Jill A. Warden can be reached on 571-272-1267. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

**/William H. Beisner/
Primary Examiner
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WHB

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